indicated that claims 40-49 are free of any prior art rejections. For reasons detailed below, the objections and rejection of the claims should be withdrawn.

1. The Claims are Definite

Claims 25-57 are rejected under 35 U.S.C. § 112, second paragraph. The Examiner alleges that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, Claim 24, 25 and 40 are rejected because the recitation of the following phrase "capable of" are said to renders the claims indefinite. Claims 32, 53 and 55 are rejected because the claims are said to be written in the past tense thereby rendering them vague and indefinite.

Applicants have amended Claims 24, 25 and 40 to delete the phrase "capable of." Claims 32, 53 and 55 have been amended to recite the active tense rather than the past tense. The claims have been amended to address each of the rejections cited by the Examiner. In view of the foregoing amendments to the claims, the rejections under 35 U.S.C. §112, second paragraph, should be withdrawn.

2. The Claims Are Not Anticipated Under 35 U.S.C. § 102(b)

Claims 24-26, 28 and 32-39 are rejected under 35 U.S.C. § 102(b) as anticipated by Bottini et al. (1996, European J. of Immunology 26:1816-1824; "Bottini"). The Examiner alleges that Bottini teaches an *in vitro* method of determining the repertoire of NKR immunoreceptors comprising the KIR p58 and the KAR p50 target

NY02:342094.1 -15-

receptors. According to the Examiner, Bottini teaches an *in vitro* method characterized in that at least one of the 3' and 5' oligonucleotide pair hybridizes to the target receptor only. Further, the Examiner maintains that Bottini teaches an *in vitro* method characterized in that the 5' oligonucleotide of the 3' and 5' oligonucleotide pair used for an NKR target receptor hybridizes to the DNA or to the cDNA of an NKR receptor counterpart (Figure 8 of Bottini).

Invalidity for anticipation requires that all of the elements and limitations of the claim be found within a single prior art reference. There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. Scripps *Clinic Research & Foundation v.*Genentech Inc., 927 F.2d 1585, 18 U.S.P.O. 2d 1001 (Fed. Cir. 1991).

In the present instance, the question is whether Bottini teaches methods for amplification of the particular target immunoreceptors <u>specified</u> in the claims, *i.e.*, the p58.1, p58.2, p70.INH, p140.INH, NKG2A, NKG2B, 50.1, 50.2, p70.ACT, p140.ACT, NKG2C, NKG2D, NKG2E and NKG2F receptors. Clearly the answer to this question is no.

As asserted in Applicant's prior response filed on August 28, 2001, Bottini discloses the identification of a novel p50 NK receptor referred to as pKKA3. As indicated by the amino acid sequences presented in Figure 10, pKKA3 is <u>different</u> from the amino acid sequences of the p58.1, p58.2, p50.1 and p50.2 NK receptors. As set forth in Bottini, the PAX mAb specifically recognize the NK receptor referred to as the pKKA.3 immunoreceptor while the EB6 antibody recognizes the p58.1 and p50.1 receptor and the GL183 antibody recognizes the p58.2 and p50.2 receptor. The PCR

NY02:342094.1 -16-

amplification demonstrated in Figure 8 of Bottini represents amplification using cDNA derived from a PAX⁺ EB6⁻GL183⁻NK cloned cell line. However, since the cell line from which the cDNA was derived lacks EB6 and GL183 reactivity, the amplification depicted in Figure 8 cannot be amplification of the p50.1, p50.2 p58.1 or p58.2. Therefore, Bottini fails to disclose pairs of oligonucleotide primers that may be used to selectively amplified the target NKR immunoreceptors encompassed by Applicant's claims.

The Examiner alleges that the features upon which Applicants rely on to distinguish the claimed invention from Bottino are not recited in the claims. Applicants respectfully disagree with the Examiner's contention regarding the pending claims. For example, Claim 24 is clearly limited to "identifying the repetoire of NKR inhibitory immunoreceptors selected from the group consisting of p58.1, p58.2, p70.INH, p140.NH, NKG2A and NKG2B receptors." Further, step (i) of the claim is limited to the use of oligonucleotides that specifically bind to the specified target receptors. In addition, claim 25 is clearly limited to "identifying the repetoire of NKR activatory immunoreceptors selected from the group consisting of p50.1, p50.2, p70.ACT, p140.ACT, NKG2C and NKG2D, NKG2E and NKG2F receptors."

Bottini clearly <u>fails</u> to disclose a method for detecting the <u>specific</u> receptors to which the claims are limited. Thus, given the differences between the presently claimed invention and the disclosure of Bottini, the invention cannot be anticipated.

NY02:342094.1 -17-

3. The Claims Are Not Anticipated Under 35 U.S.C. § 102(a)

Claims 24-25, 29-30 and 32-39 are rejected under 35 U.S.C. § 102(a) as being anticipated by Hiby et al. (1997, Molecular Immunology, 34:419-430; "Hiby").

The Examiner alleges that Hiby teaches an *in vitro* method of documenting a repertoire of NKR inhibitory or activatory immunoreceptors comprising the KIR p58.2, p58.1, KAR p50.2 and 50.1 target receptors.

As indicated above, anticipation requires that all the elements and limitations of the claim be found within a single prior art reference. Scripps, *supra*.

A review of Hiby indicates that Hiby merely discloses that human uterine NK cells have a similar repertoire of KIR and KAR receptors expressed on their surface as those found in blood. The study was conducted using RT-PCR and sequencing. The primers utilized in the study, as depicted in Figure 1 and Table 1, were capable of amplifying all KIR and KAR receptors based on sequences conserved between the different types of receptors. While the selected primers were capable of distinguishing between receptors with two Ig-SF extracellular domains versus those with three Ig-SF domains, Hiby fails to disclose pairs of oligonucleotide primers that could be used to selectively amplify specific target receptors. Indeed, the present invention is based on Applicant's discovery for the first time of oligonucleotide primers capable of selective amplification of a target receptor, *i.e.*, p58.1, p58.2, p70.INH, p140.INH, NKG 2A, NKG 2B, p50.1, p50.2, p70.ACT, p140.ACT, NKG 2C, NKG 20, NKG 2E and NKG 2F.

It is essential to note that in the present invention mere detection of hybridization between a nucleic acid encoding an NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair, due to their unique specificity, results in identification

NY02:342094.1 -18-

of a target receptor. Furthermore, the claim specifies that <u>detection of hybridization</u> identifies the repetoire of NKR inhibitory receptors. In contrast, Hiby requires <u>sequencing</u> of the amplified fragments to identify the receptor. Thus, the data presented in Table 3 is derived from sequencing of the amplified fragments.

The Examiner maintains that in the presence of the open "comprising" language of the claim, any additional step may be included in the method, including sequencing of the target DNA molecules as taught by Hiby.

Applicants assert that in the present instance, the claim is directed to a method for identifying the repetoire of NKR immunoreceptors which is based on the mere detection of hybridization between nucleic acid molecules encoding the NKR immunoreceptor and 3' and 5' oligonucleotides. Invalidity for anticipation requires that all of the elements and limitations of the claim be found within a single prior art reference. As indicated above, there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. Scripps *Clinic Research & Foundation v. Genentech Inc.*, 927 F.2d 1585, 18 U.S.P.Q. 2d 1001 (Fed. Cir. 1991). Higby simply does not teach a method, for identifying the repetorie of NKR immunoreceptors based on the detection of hyridization.

Thus, given the differences between Hiby and the present invention,
Applicants respectfully request withdrawal of the 102(a) rejection.

4. The Claim Invention Is Not Obvious

Claims 24-28, and 32-39 are rejected under 35 U.S.C. §103 over Bottino in view of Matthews et al. (Analytical Biochemistry, 1988, 169:1-25). According to the

NY02:342094.1 -19-

Examiner, Bottino teaches the method of claims 24-26, 28 and 32-39 and Matthews teaches a fluorescent marker. According to the Examiner, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute and combine a fluorescent marker of Matthews with the method of Bottino.

Claims 24-26 and 28-39 are rejected under 35 U.S.C.§103 over Bottino in view of Badman et al. (U.S. Patent 6,307,021 B1). According to the Examiner, Bottino teaches the method of claims 24-26, 28 and 32-39 and Badman teaches a method where amplification is by nested PCR using a DNA polymerase. The Examiner alleges that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute and combine amplification by PCR with the method of Bottino.

Claims 24-26, 28, 32-39 and 50-55 are rejected under 35 U.S.C §103 over Bottino, in view of Finkel (U.S. Patent 5,976,819). The Examiner alleges that Bottino teaches the method of claims 24-26, 28 and 32-39 and Finkel teaches a method used to predict the acceptance or rejection by a subject of tissue. According to the Examiner, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute and combine the method used to predict the acceptance or rejection by a subject of tissue of Finkel with the method of Bottino.

Applicants respectfully disagree with the Examiner's rejection and submit that the claimed invention is not rendered obvious by the cited art using the objective standard for obviousness under 35 U.S.C. §103. As set forth in *Graham v. Deere*, a finding of obvious ness under 35 U.S.C. §103 requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the

NY02:342094.1 -20-

claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. John Deere, Inc.* 383 U.S. 1 (1966).

In the present instance, the proper inquiry is whether the cited references suggest the claimed *in vitro* methods for identifying the repetoire of NKR immunoreceptors within a subject. Applicants assert that the answer to this question is no. Bottino only discloses the identification of a novel p50 NKR receptor referred to as pKKA3 which is a different receptor from the receptors specified in the pending claims. Bottino <u>fails</u> to disclose that oligonucleotide primers may be used to selectively target hybridization to the target NKR immunoreceptors, much less the structure of such oligonucleotides. Furthermore, Applicants assert that there is nothing in the additionally cited references, *i.e.*, Matthews, Bandman or Finkel, that "fills the gap" in the teaching of Bottino. Therefore, the claimed invention is not obvious, and the rejection under 35 U.S.C.§103 should be withdrawn.

CONCLUSION

Entry of the foregoing amendments and remarks into the file of the above identified application is respectfully requested. The Applicants believe that the invention described and defined by the amended claims is patentable over the rejections of the

NY02:342094.1 -21-

Examiner. Withdrawal of all rejections and reconsideration of the new claims is requested. An early allowance is earnestly sought.

Respectfully submitted,

Dated: Decmber 16, 2002

Currelly Y. Gliphurs

John Murnane Patent Office Reg. No.

Carmella L. Stephens Patent Office Reg. No. 41,321

BAKER BOTTS L.L.P. 30 Rockefeller Plaza New York, New York 10112-0228

Attorneys for Applicant (212) 408-2500

NY02:342094.1 -22-

APPENDIX A

--24. (New) An *in vitro* method for identifying the repertoire of NKR inhibitory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p58.1, p58.2, p70.INH, p140.NH, NKG2A and NKG2B receptors, these immunoreceptors being designated hereinafter target receptors, comprising:

- (i) contacting a nucleic acid sample derived from said subject with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, wherein the 3' and 5' oligonucleotides [of the same said pair both being capable of hybridization] hybridize in a buffer comprising 20 mM Tris-HC1, pH 8.4; 50 mM KCl; 2.5 mM MgCl₂ at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but not hybridizing, under the same hybridization conditions, with a NKR activatory immunoreceptor counterpart and;
- (ii) detecting hybridization between the nucleic acid encoding the

 NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide

 pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair(s)identifies the repetoire of NKR inhibitory receptors.

NY02:342094.1 -23-

25. (New) An *in vitro* method for identifying the repertoire of NKR activatory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p50.1, p50.2, p70.ACT. p140.ACT, NKG2C, NKG2D, NKG2E and NKG2F, these immunoreceptors being designated hereinafter target receptors, comprising:

- with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, wherein the 3' and 5' oligonucleotides [of the same said pair both being capable of hybridization]

 hybridize in a buffer comprising 20 mM Tris-HC1, pH 8.4;

 50 mM KCl; 2.5 mM MgCl₂ at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but not hybridizing, under the same hybridization conditions, with a NKR inhibitory immunoreceptor counterpart:and;
- (ii) detecting hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s)identifies the repetoire of NKR activatory receptors.

NY02:342094.1 -24-

- 32. (Amended) The method of claim 24 or 25 wherein the hybridization [which may be formed comprises, in addition, the resolution, on a polyacrylamide gel, of the reaction mixture derived from the bringing into contact, as well as the visualization of the presence or of the absence of electrophoretic bands containing the said hybrids which may be formed] between the nucleic acid molecule encoding the NKR activatory or inhibitory immunorecptors and the 3' and 5' oligonucleotide pairs is detected by resolution and visualization on a polyacrylamide gel of electrophoretic bands containing the said hybrids.
- 54. (Amended) The method of claim 24 or 25 wherein said method is used to predict or monitor the state of resistance of a subject to (i) infection, wherein said infection is viral, [such as an HIV infection, or a] parasitic [infection, such as malaria], or [a] bacterial [infection, towards] (ii) autoimmune disease, [such as rheumatoid arthritis,] or [alternatively towards] the development of malignant cells [such as leukemia cells].
- 55. (Amended) The method of claim 24 or 25 wherein said method is used to screen for compositions which can be used to reduce the symptoms associated with infectious, autoimmune or proliferation disorders.

Please add the following new claims:

--58. (New) An *in vitro* method for identifying the repertoire of NKR inhibitory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p58.1, p58.2, p70.INH, p140.NH, NKG2A and NKG2B

NY02:342094.1 -25-

receptors, these immunoreceptors being designated hereinafter target receptors, comprising:

- (i) contacting a nucleic acid sample derived from said subject with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, and wherein the 3' and 5' oligonucleotides hybridize in a buffer comprising 20 mM Tris-HC1, pH 8.4; 50 mM KCl; 2.5 mM MgCl₂ at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but do not hybridize, under the same hybridization conditions, with a NKR activatory immunoreceptor counterpart and wherein;
 - (a) the 5' oligonucleotide comprises the sequence of SEQ ID No.1, and at least one 3' oligonucleotide selected from the group of 3' oligonucleotides comprising the sequence of SEO ID No. 5, No. 2, No. 6 or No. 7; or
 - (b) the 5' oligonucleotide comprises the sequence of SEQ ID

 No. 4 and at least one 3' oligonucleotide selected from the
 group of 3' oligonucleotide comprising the sequence of

 SEQ ID No. 5, No. 2, No. o or No. 7, or a sequence which
 is derived therefrom; or
 - (c) the 5' oligonucleotide comprises the sequence of SEQ ID

 No. 9, or a sequence which is derived therefrom, and at

NY02:342094.1 -26-

least one 3' oligonucleotide selected from the group of 3' oligonucleotides comprising the sequence SEQ ID No. 5, No. 2, No. 6 or No. 7, or a sequence which is derived therefrom; or.

- (d) at least one 5' oligonucleotide comprising the sequence of SEQ ID No. 10, No. 11, No. 12 or No. 13 is selected from the group consisting of a 3' oligonucleotide comprising the sequence SEQ ID No. 14, or a sequence which is derived therefrom; and
- (ii) detecting hybridization between the nucleic acid encoding the

 NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide

 pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair(s)identifies the repetoire of NKR inhibitory receptors.

59. (New) An *in vitro* method for identifying the repertoire of NKR activatory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p50.1, p50.2, p70.ACT. p140.ACT, NKG2C, NKG2D, NKG2E and NKG2F, these immunoreceptors being designated hereinafter target receptors, comprising:

NY02:342094.1 -27-

- with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, wherein the 3' and 5' oligonucleotides hybridize in a buffer comprising 20 mM Tris-HC1, pH 8.4; 50 mM KCl; 2.5 mM MgCl₂ at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but do not hybridize, under the same hybridization conditions, with a NKR inhibitory immunoreceptor counterpart and wherein;
 - the 3' oligonucleotide of a said 3' and 5' oligonucleotide pair, used for determining the repertoire of NKR activatory immunoreceptors, is capable, under the same said hybridization conditions, of hybridizing to a nucleic acid encoding KAR target receptor wherein said nucleic acid encodes the amino acid sequence Lys Ile Pro Phe Thr Ile (K I P F T I) or Lys Leu Pro Phe Thr Ile (K L P F T I) (SEQ ID No. 26 or 27); or
 - (b) the 5' oligonucleotide comprises the sequence of SEQ ID

 No. 1 and a 3' oligonucleotide comprising the sequence of

 SEQ ID No. 3;or

NY02:342094.1 -28-

- (c) the 5' oligonucleotide comprises the sequence of SEQ ID

 No. 8 and a 3' oligonucleotide comprising the sequence of

 SEQ ID No. 3; or
- (d) the 5' oligonucleotide comprising the sequence of SEQ ID

 No. 9 and a 3' oligonucleotide comprising the sequence

 SEQ ID No. 3; or
- (e) the 5' oligonucleotide comprises the sequence of SEQ ID

 No. 15 and a 3' oligonucleotide comprising the sequence

 SEQ ID No.13; and
- (ii) detecting hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s)identifies the repetoire of NKR activatory receptors.

60. (New) An *in vitro* method for identifying the repertoire of NKR inhibitory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p58.1, p58.2, p70.INH, p140.NH, NKG2A and NKG2B receptors, these immunoreceptors being designated hereinafter target receptors, comprising:

NY02:342094.1 -29-

(i) contacting a nucleic acid sample derived from said subject with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, and wherein the 3' and 5' oligonucleotides hybridize in a buffer comprising 20 mM Tris-HC1, pH 8.4; 50 mM KCl; 2.5 mM MgCl₂ at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but do not hybridize, under the same hybridization conditions, with a NKR activatory immunoreceptor counterpart and wherein said 3' and 5' oligonucleotide pairs are selected from the group consisting of:

- (a) a 5' oligonucleotide comprising the sequence of SEQ ID

 No. 16 and a 3' oligonucleotide comprising the sequence

 SEQ ID No. 17;
- (b) a 5' oligonucleotide comprising the sequence of SEQ ID

 No. 18 and a 3' oligonucleotide comprising the sequence

 SEQ ID No. 17;
- (c) a 5' oligonucleotide comprising the sequence of SEQ ID

 No. 19 and a 3' oligonucleotide comprising the sequence

 SEQ ID No. 17; and
- (d) a 5' oligonucleotide comprising the sequence of SEQ ID

 No. 20 and a 3' oligonucleotide comprising the sequence

 SEQ ID No. 21; and

NY02:342094.1 -30-

(ii) detecting hybridization between the nucleic acid encoding the

NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide

pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR inhibitory immunoreceptor and the 3' and 5' oligonucleotide pair(s)identifies the repetoire of NKR inhibitory receptors.

- 61. (amended) An *in vitro* method for identifying the repertoire of NKR activatory immunoreceptors within a subject wherein said immunoreceptors are selected from the group consisting of p50.1, p50.2, p70.ACT. p140.ACT, NKG2C, NKG2D, NKG2E and NKG2F, these immunoreceptors being designated hereinafter target receptors, comprising:
 - with at least one pair of oligonucleotides, one being designated a 3' oligonucleotide and the other a 5' oligonucleotide, wherein the 3' and 5' oligonucleotides hybridize in a buffer comprising 20 mM Tris-HC1, pH 8.4; 50 mM KCl; 2.5 mM MgCl₂ at a temperature of between 50°C and 65°C, to a nucleic acid encoding a target receptor, but do not hybridize, under the same hybridization conditions, with a NKR inhibitory immunoreceptor counterpart and wherein said 3' and 5' oligonucleotide pairs are selected from the group consisting of:

NY02:342094.1 -31-

- (a) a 5' oligonucleotide comprising the sequence of SEQ ID

 No. 16 and a 3' oligonucleotide comprising the sequence

 SEQ ID No. 17;
- (b) a 5' oligonucleotide comprising the sequence of SEQ ID

 No. 18 and a 3' oligonucleotide comprising the sequence

 SEQ ID No. 17;
- (c) a 5' oligonucleotide comprising the sequence of SEQ ID

 No. 19 and a 3' oligonucleotide comprising the sequence

 SEQ ID No. 17; and
- (d) a 5' oligonucleotide comprising the sequence of SEQ ID

 No. 20 and a 3' oligonucleotide comprising the sequence

 SEQ ID No. 21; and
- (ii) detecting hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s),

wherein detection of hybridization between the nucleic acid encoding the NKR activatory immunoreceptor and the 3' and 5' oligonucleotide pair(s)identifies the repetoire of NKR activatory receptors.

62. (New) The method of claim 58, 59, 60 or 61 wherein said method is used to predict or to monitor the acceptance or rejection, by a subject, of cells, tissue or organ which are genetically different.

NY02:342094.1 -32-

- 63. (New) The method according to claim 58, 59, 60 or 61 wherein said method is used to predict or to monitor the safety or the pathogenicity (GVH), for a subject, of a graft or transplant, of cells, tissue or organ which are genetically different.
- 64. (New) The method according to claim 58, 59, 60 or 61 wherein said method is used to predict or to monitor for a subject of a GVL-type effect on the part of cells, tissue or organ which are genetically different.
- 65. (New) The method of claim 58, 59, 60 or 61 wherein said method is used to determine the state of activation of NK and/or T cells within a subject.
- 66. (New) The method of claim 58, 59, 60 or 61 wherein said method is used to predict or monitor the state of resistance of a subject to (i) infection, wherein said infection is viral, parasitic or bacterial (ii) autoimmune disease, or (iii) the development of malignant cells.
- 67. (New) The method of claim 58, 59, 60 or 61 wherein said method is used to screen for compositions which are used to reduce the symptoms associated with infectious autoimmune or proliferation disorders.
- 68. (New) A kit for carrying out the method of claim 58, 59, 60 or 61 comprising a container, at least one said 3' and 5' oligonucleotide paid, and reagents for carrying out the said method.
- 69. (New) The kit of claim 68 wherein said 3' and 5' oligonucleotide pair is coupled to a marker.

NY02:342094.1 -33-

- 70. (New) The method of claim 58, 59, 60 or 61 wherein the 3' or 5' oligonucleotides are coupled to a marker, allowing detection of hybridization between the nucleic acid sample and the 3' and 5' oligonucleotides.
- 71. (New) The method of claim 70 wherein the marker is a fluorescence marker.
- 72. (New) The method of claim 70 wherein the marker is a radioactive marker.
- 73. (New) The method of claim 58, 59, 60 or 61 wherein the 3' and 5' oligonucleotide pair(s) serve(s) as 3' and 5' primers, respectively, for extension by DNA polymerase.
- 74. (New) The method of claim 58, 59, 60 or 61 wherein hybridization between the nucleic acid sample and the 3' and 5' oligonucleotide pair is detected by PCR amplification.
- 75. (New) The method of claim 58, 59, 60 or 61 wherein amplification is by nested PCR.
- 76. (New) The method of claim 58, 59, 60 or 61 wherein the hybridization between the nucleic acid molecule encoding the NKR activatory or inhibitory immunoreceptors and the 3' and 5' oligonucleotide pairs is detected by resolution and visulaization on a polyacrylamide gel and visualization of electrophoretic bands containing the said hybrids.

NY02:342094.1 -34-

- 77. (New) The method of claim 58 wherein said method is used to document the genotypic repertoire of KIR immunoreceptors.
- 78. (New) The method of claim 58 wherein said method is used to document the expression repertoire of KIR immunoreceptors.
- 79. (new) The method of claim 59 wherein said method is used to document the genotypic repertoire of KAR immunoreceptors.
- 80. (New) The method of claim 59 wherein said method is used to document the expression repertoire of KAR immunoreceptors.
- 81. (New) The method of claim 58, 59, 60 or 61 wherein the nucleic acid sample is of human or animal origin.
- 82. (New) The method of claim 58, 59, 60 or 61 wherein the nucleic acid sample is derived from blood, bone marrow, lymphocytes, NK and/or T cells or transgenic cells.
- 83. (New) The method of claim 58, 59, 60 or 61 wherein the nucleic acid sample is a genomic or cDNA library.--

NY02:342094.1 -35-